

## Advanced Brain MR Imaging

### **Surgical Planning of Tumors with fMRI and DTI**

Alberto Bizzi, M.D.

Recent significant technical advances in neuroimaging modalities are changing the standards for preoperative imaging and surgical planning of patients with a brain tumor. The goal of every neurosurgical procedure is to maximize tumor resection with minimal permanent postoperative neurological morbidity. The extent of resection depends on tumor's location, size, presumed diagnosis on morphological MRI, age and medical conditions of the patient. Advances in neurosurgical methods, including frameless navigational systems, intraoperative imaging with ultrasonography or intraoperative MR imaging (iMRI), and electrostimulation mapping techniques (ESM) enable the neurosurgeon to optimize cytoreduction. Neuronavigation systems assist the neurosurgeon in planning the approach to the tumor and in evaluating the extent of cytoreduction.

Resection of a lesion near eloquent functioning cortex and white matter tracts requires a detailed understanding of functional anatomy and its relationship to surrounding cortical gray matter and white matter connections. Intraoperative ESM of cortical and subcortical tissue in and around a tumor has been used to identify functional tissue. ESM is the only technique available that provides reliable identification of subcortical tracts carrying motor, sensory and language informations.

Functional MRI (fMRI) has been used in the presurgical localization of eloquent gray matter structures near brain tumors. Multiple fMRI studies have shown that small changes in blood oxygenation occur in

eloquent cortex during execution of a task. Unfortunately, several uncontrolled biological and physiological variables make the interpretation of fMRI studies sometimes difficult. Loss of neurovascular autoregulation in areas of functioning brain tissue adjacent to the tumor may be the cause of false negative results. The difficulty to differentiate homotopic reorganization from pseudo-reorganization may be another cause of confusion.

The accuracy of the BOLD response in mapping eloquent functional cortex has been evaluated using intraoperative ESM or magnetoencephalography (MEG) as a gold standard. Many studies have shown that fMRI is pretty good to identify the primary motor (PMC), primary sensory (PSC) and primary visual cortex. It is good but not perfect to map the language network. fMRI is not accurate enough to lateralize memory functions. When fMRI results are discordant it is very important that the neuroradiologist recommend the use of alternate techniques such as ESM, MEG, Wada to confirm functional relationships. A systematic follow-up of the neurological exam of the patient post-surgery is also essential in evaluating the accuracy of fMRI. The neuroradiologist must acknowledge the limitations of the technique during analysis of the results.

Another limitation of fMRI is its insensitivity to functional white matter tracts that may be within or around the neoplasm. Diffusion Tensor Imaging (DTI) has the potential to provide this type of information preoperatively. DTI is based on the principle of anisotropic diffusion of water in axons and compacted fiber bundles. The spatial orientation of major (compacted) fiber tracts can then be represented with color-coded directional maps. White matter tracts with a craniocaudal orientation are displayed in blue; tracts with a left/right orientation in red; tracts with an anterior/posterior orientation in green. The

accuracy of DTI-based color-coded maps to identify functioning white matter surrounding an infiltrating neoplasm is currently under investigation. It has been proposed that the combination of fractional anisotropy (FA) and orientation measures provided by DTI allows characterization of white matter tracts in four categories: displaced, edematous, infiltrated and destroyed. These informations also may be very useful to the neurosurgeon.

Studies combining fMRI and DTI-based tractography use ROI defined by fMRI instead of *a priori* ROI to look for white matter bundles connecting activated cortical areas of a specified network. The main clinical indication of combining fMRI with DTI is a cerebral neoplasm located within or adjacent the primary motor or language areas.

Eloquent structures of the motor network include the precentral and postcentral cortex (motor strip), the Supplementary Motor Area (SMA), and the pyramidal tracts connecting the motor strip throu the posterior limb of the internal capsule to the brainstem. Eloquent cortical areas and fiber bundles that form the language network are the inferior frontal gyrus (IFG, that is also known as Broca's area), the dorsolateral prefrontal cortex (DLPFC), the anterior cingulate, the posterior superior temporal gyrus (STG, that is also known as Wernicke's area) and the uncinate fasciculus.

The limitations of fMRI and DTI in preoperative imaging of brain tumors and other issues related to technical and clinical validation of these techniques before they can be translated into clinical practice will also be addressed.

Alberto Bizzi, M.D.  
Dept. of Neuroradiology  
Istituto Nazionale Neurologico "Carlo Besta"  
Via Celoria, 11

### **Suggested readings**

1. Keles GE and Berger MS. Advances in Neurosurgical technique in the current management of brain tumors. *Seminars in Oncology* 2004; 31:659-665.
2. Ojemann G, Ojemann J, Lettich E, Berger M. Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. *J Neurosurg* 1989; 71(3):316-326.
3. Yetkin FZ, Mueller WM, Morris GL, McAuliffe TL, Ulmer JL, Cox RW, Daniels DL, Haughton VM. Functional MR activation correlated with intraoperative cortical mapping. *AJNR* 1997; 18(7):1311-5.
4. Liu W-C, Feldman SC, Schulder M et al. The effect of tumour type and distance on activation in the motor cortex. *Neuroradiology* 2005; 47:813-819.
5. Kim MJJ, Holodny AI, Hou BL et al. The effect of prior surgery on BOLD fMRI in the preoperative assessment of brain tumors. *AJNR* 2005; 26:1980-1985.
6. Ulmer JL, Krouwer HG, Mueller WM et al. Pseudo-reorganization of language cortical function at fMRI: a consequence of tumor-induced neurovascular uncoupling. *AJNR* 2003; 24:213-217.
7. Ulmer JL, Hacein-Bey L, Mathews VP, et al. Lesion-induced pseudo-dominance at functional magnetic resonance imaging: implications for preoperative assessments. *Neurosurgery*. 2004;55(3):569-79.
8. Petrovich N, Holodny AI, Tabar V et al. Discordance between fMRI during silent speech tasks and intraoperative speech arrest. *J Neurosurg* 2005; 103:267-274.
9. Fernandez G, Specht K, Weis S et al. Intrasubject reproducibility of presurgical language lateralization and mapping using fMRI. *Neurology* 2003; 60:969-975.
10. Herholz K, Reulen HJ, von Stockhausen HM, Thiel A, Ilmberger J, Kessler J, Eisner W, Yousry TA, Heiss WD. Preoperative activation and intraoperative stimulation of language-related areas in patients with glioma. *Neurosurgery*. 1997;41(6):1253-60; discussion 1260-2.

11. FitzGerald DB, Cosgrove GR, Ronner S et al. Location of language in the cortex: a comparison between fMRI and electrocortical stimulation. *AJNR* 1997; 18:1529-1539.
12. Lurito JT, Lowe MJ, Sartorius C, Mathews VP. Comparison of fMRI and intraoperative direct cortical stimulation in localization of receptive language areas. *J Comput Assist Tomogr* 2000; 24(1):99-105.
13. Roux FE, Boulanouar K, Lotterie JA et al. Language fMRI in preoperative assessment of language areas: correlation with direct cortical stimulation. *Neurosurgery* 2003; 52:1335-1347.
14. Roux FE, Ibarrola D, Lotterie JA, Chollet F and Berry I. Perimetric visual field and fMRI correlation: implications for image-guided surgery in occipital brain tumors. *JNNP* 2001; 71:505-514.
15. Conturo TE, Lori NF, Cull TS et al. Tracking neuronal fiber pathways in the living human brain. *PNAS* 1999; 96:10422-10427.
16. Jellison BJ, Field AS, Medow J et al. DTI of cerebral white matter: a pictorial review of physics, fiber tract anatomy, and tumor imaging patterns. *AJNR* 2004; 25:356-369.
17. Wakana S, Jiang H, Nagae-Poetscher LM, van Zijl PC, Mori S. Fiber tract-based atlas of human white matter anatomy. *Radiology* 2004; 230:77-87.
18. Witwer BP, Moftakhar R, Hasan KM et al. DTI of white matter tracts in patients with cerebral neoplasm. *J Neurosurg* 2002; 97:568-575.
19. Ulmer JL, Salvan CV, Mueller WM et al. The role of DTI in establishing the proximity of tumor borders to functional brain systems: implications for preoperative risk assessments and postoperative outcomes. *Technology in Cancer Research & Treatment* 2004; 3(6):567-576.
20. Thomalla G, Glauche V, Koch MA et al. DTI detects early Wallerian degeneration of the pyramidal tract after ischemic stroke. *NeuroImage* 2004; 22:1767-1774.
21. Holodny AI, Ollenschleger MD, Liu WC, Schulder M, and Kalnin AJ. Identification of the corticospinal tracts achieved using BOLD and diffusion functional MRI in patients with brain tumors. *AJNR Am J Neuroradiol.* 2001 Jan;22(1):83-8.
22. Holodny AI, Gor DM, Watts R et al. Organization of corticospinal tracts in the internal capsule: initial anatomic results in contradistinction to prior reports. *Radiology* 2005; 234:649-653.
23. Kier EL, Staib LH, Davis LM, Bronen RA. MR imaging of the temporal stem: anatomic dissection tractography of the uncinate fasciculus, inferior occipitofrontal fasciculus, and Meyer's loop of the optic radiation. *AJNR* 2004; 25:677-691.
24. Hendler T, Pianka P, Sigal M et al. Delineating gray and white matter involvement in brain lesions: three-dimensional alignment of fMRI and DTI. *J Neurosurg* 2003; 99:1018-1027.

25. Guye M, Parker GJM, Symms M et al. Combined fMRI and tractography to demonstrate the connectivity of the human primary motor cortex in vivo. *NeuroImage* 2003; 19: 1349-1360.
26. Kim D-S, Kim M, Ronen I et al. In vivo mapping of functional domains and axonal connectivity in cat visual cortex using MRI. *Magnetic Resonance Imaging* 2003; 21: 1131-1140.
27. Berman JI, Berger MS, Mukherjee P, Henry RG. DTI-guided tracking of fibers of the pyramidal tract combined with intraoperative cortical stimulation mapping in patients with gliomas. *J Neurosurg* 2004; 101: 66-72.
28. Henry RG, Berman JI, Nagarajan SS et al. Subcortical pathway serving cortical language sites: initial experience with DTI fiber tracking combined with intraoperative language mapping. *NeuroImage* 2004; 21: 616-622.
29. Nimsky C, Ganslandt O, Hastreiter P, Wang R, Benner T, Sorensen AG and Fahlbusch R. Intraoperative DT-MRI: shifting of white matter tracts during neurosurgical procedures – initial experience. *Radiology*. 2005 Jan; 234(1): 218-25.
30. Ulmer JL and Holodny AI. Functional neuroradiology: a call to action. *AJNR* 2005; 26: 2-3.